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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/774,843	PELED ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *401-463* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *401-463* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-400 are canceled. Claim 401-463 are pending in the instant application.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 401, 411-412, 414-425, 434, 436-453, 455, 460-462, drawn to methods of ex vivo expansion of stem cells and an expanded stem cell preparation, classified in class 435, subclasses 375 and 325.

II. Claims 402-403, and 407, drawn to methods of transplantation, classified in class 424, subclass 93.1.

III. Claims 404-406, drawn to a genetically modifying stem cells with an exogene, classified in class 435, subclass 455.

IV. Claims 408-410, 426-433, 435, and 454, drawn to methods of mobilizing bone marrow stem cells in vivo by administering an agent to a donor and harvesting the cells, classified in class 424.

V. Claims 413 and 463, drawn to methods of expanding stem cells in vivo by administering an agent, classified in class 424.

VI. Claim 456, drawn to a method of preserving stem cells, classified in class 435, subclass, 374.

VII. Claim 457, drawn to a stem cell collection bag, classified in class 530 or 536.

VIII. Claim 458, drawn to a stem cell buffer, classified in class 435, subclass 404.

IX. Claim 459, drawn to an assay for determining whether an antagonist and an expansion agent, classified in class 435, subclass 4.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-IX are directed to related products and processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation. function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed are not capable of use together and have materially different designs, modes of operation and function.

Specifically, while all groups involve various types of stem cells and the use of "agents" to affect the stem cells, each method or product is materially different and does not overlap in scope with the others. For example, the products of inventions I, VII, and VIII do not overlap in scope as the stem cell preparation of invention I is not required for the collection bag or buffer of inventions VII or VIII. Further, the buffer is not required for the stem cell collection bag and vice versa. In addition, the bag and buffer are not required in any of the claimed methods and have alternative uses. Regarding the methods, the in vivo methods of administering an agent to a donor of inventions IV and V are materially different from contacting stem cells with an agent in vitro as in inventions I-III, as the in vitro methods involve the isolation and manipulation of the stem cells in tissue culture. In addition, the in vivo methods of inventions IV and V are not capable of use together as the methods of invention IV include the step of harvesting the mobilized stem cells. Further, the stem cells of invention IV are hematopoietic stem cells,

whereas the stem cells of invention V can be any stem cell, such as neural stem cell or mesenchymal stem cell and are maintained in vivo. Thus, the inventions are not capable of use together. Regarding inventions I-III, note that invention II involves the transplantation of expanded hematopoietic stem cells into a recipient, a step not required for either of inventions I or III. Note as well that the methods of I and III are not limited to hematopoietic stem cells and read on manipulating any stem cell ex vivo. Inventions I and III are also not capable of use together as the cells of invention III are genetically modified using reagents not required to expand the stem cells ex vivo. Finally, note that none of the methods of inventions I-V require the step of storing stem cells required for the methods of preserving stem cells of invention VI. Thus, each product and method is materially different from the others. It is also noted that there is nothing of record to show the inventions to be obvious variants. Therefore, for the reasons set forth above, the search for each invention is not co-extensive with any of the other inventions such that it would place an undue burden on the examiner to search and examine all inventions together.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter, different classification, and different search requirements, restriction for examination purposes as indicated is proper.

Each of inventions I-IX above require further restriction under 35 U.S.C. 121 as follows: the inventions all involve the use of multiple "agents" or a "culture conditions" set forth below, each of which represents a separately patentable invention.

A) agent or culture condition which is/includes nicotinamide or a nicotinamide analog

B) agent or culture condition which is/includes a nicotinamide derivative

C) agent or culture condition which is/includes a nicotinamide metabolite

D) agent or culture condition which is/includes a retinoic acid receptor antagonist(RAR)

E) agent or culture condition which is/includes a retinoid X receptor antagonist(RXR)

F) agent or culture condition which is/includes a Vitamin D receptor antagonist

G) agent or culture condition which is/includes a nucleic acid encoding anti-CD38

H) agent or culture condition which is/includes a nucleic acid encoding anti-RAR

I) agent or culture condition which is/includes a nucleic acid encoding anti-RXR

J) agent or culture condition which is/includes a nucleic acid encoding anti-vitamin D receptor

K) agent or culture condition which is/includes an siNA for CD38

L) agent or culture condition which is/includes an siNA for RAR

M) agent or culture condition which is/includes an siNA for RXR

N) agent or culture condition which is/includes an siNA for vitamin D receptor

Claims 401, 412, 461, and 462 link inventions I-A) - I-N).

Claims 402 and 407 link inventions II-A)-II-N).

Claim 404 links inventions III-A)-III-N).

Claim 408 links inventions IV-A)-IV-N).

Claims 413 and 463 link inventions V-A)-V-N).

Claim 456 links inventions VI-A)-VI-N).

Claim 457 links inventions VII-A)-VII-N).

Claim 458 links inventions VIII-A)-VIII-N).

Claim 459 links inventions IX-A)-IX-N).

The restriction requirement among the linked inventions is **subject to** the nonallowance of the linking claim(s) set forth above Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Methods or product using/containing each of the agents listed in inventions A)-N) are patentably distinct in that each agent has materially different chemical, structural, and biological properties from the others. As such, the search for each agent is not coextensive with the others. As such, while the methods are related, each method is mutually exclusive based on the use of the agent and the methods do not overlap in scope and are not obvious variants. Therefore, it would place an undue burden on the examiner to search and examiner all inventions together.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter, and different search requirements, restriction for examination purposes as indicated is proper.

This application further contains claims directed to the following patentably distinct species:

1) species of cytokine, see for example claim 410 which lists 14 different species and also claim 424 which lists additional cytokine species

2) species of siNA, see for example claim 433 which lists 4 different species

3) species of nicotinamide analogs, see for example claim 437 which lists 4 different species

4) species of RAR antagonists, see for example claim 442 which lists numerous species

5) species of RXR antagonists, see for example claim 443 which lists numerous species

6) species of vitamin D receptor antagonists, see for example claim 444, which lists numerous species.

The species are independent or distinct because each cytokine, siNA, nicotinamide analog, RAR antagonist, RXR antagonist, and vitamin D receptor antagonist is chemically, structurally, and functionally different from the others such that the search for one species would not be coextensive with any of the other species. As such, it would place an undue burden on the examiner to search and examine all species together.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species from each of 1)-g) for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note

that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

Dr. A.M.S. Wehbé